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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/706,301	11/03/2000	Koichi Saito	207198	6724

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/706,301	SAITO ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. In view of the Appeal Brief filed on 2/17/04, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(a) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(b) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

2. Claims 1-17 are pending and being acted upon.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-17 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed vaccine could function for the treatment or prevention of the diseases/conditions that would be encompassed by the claims. Note that the rejection as it regards how to make the vaccines of the instant claims has been withdrawn.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding novel methods involving biological processes, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)". The MPEP further states that physiological activity can be considered inherently unpredictable. Accordingly, significant enablement, representative of the scope of the claimed vaccines, would be required.

It is noted that the claimed invention is intended to encompass significant breadth, i.e., vaccines for the prevention or treatment of *any and all* types of infection, including but not limited to, bacterial, viral, fungal, and parasitic infections, as well as tumor vaccines. Note that the specification discloses essentially no limitations on the vaccines encompassed by the claims. Indeed, the specification discloses that any "inactivated cells, inactivated viral particles, inactivated Mycoplasma [can] generally [be] used, as well as pathogen infection preventive factor, such as attachment protein, envelope antigen and the like used for subunit vaccine, are used." Again, given the breadth of the claims significant enablement would be required.

A review of the specification discloses just two relevant examples, both employing the same antigen. Experimental Example 1 discloses that a vaccine of swine erysipelas had some efficacy in a mouse disease model. It is unclear precisely what Experimental Example 2 is intended to demonstrate, but it appears that immunized and infected animals are asserted to have "decreased [but still present] lung lesions" in comparison to control infected animals. This limited disclosure cannot be considered to be representative (nor enabling) of the scope of the claims for the following reasons.

Regarding tumor vaccines (which would be encompassed by the vaccines of the instant claims given the lack of limitations), while positive results have been achieved versus tumor associated antigens (TAAs) in some animal models, said achievements do not generally correlate with positive results in humans (i.e., the most likely intended subject for the claimed vaccines). As taught by Bodey et al. (2000) the reasons are relatively straight-forward:

"The theoretical basis for all of these approaches [immunotherapy] is very well founded. Animal models, albeit highly artificial, have yielded promising results. Clinical trials in humans, however, have been somewhat disappointing. Although general immune activation directed against the target antigens contained within the cancer vaccine has been documented in most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccines to fulfill their promise is due to the very relationship between host and tumor; through a natural selection process the host leads to the selective enrichment of clones of highly aggressive neoplastically transformed cells, which apparently are so dedifferentiated that they no longer express cancer cell specific molecules. Specific activation of the immune system in such cases only leads to lysis of the remaining cells expressing the particular TAAs in the context of the particular human leukocyte antigen (HLA) subclass and the necessary costimulatory molecules. The most dangerous clones of tumor cells however lack these features and thus the cancer vaccine is of little use."

Indeed this selection for the most aggressive tumor cells would likely exacerbate disease in the long run. At any rate, the reference demonstrates that significant enablement would be required for claims encompassing tumor vaccines.

Regarding formulations which induce effective anti-virally infected cell immunity (an embodiment specifically disclosed at page 9 of the specification), even less is known. Indeed, as taught by Cohen (2002) it is not yet even known whether a CTL response against a virus such as HIV is even technically capable of providing effective immunity. See also Cohen (2004) in which it is taught that an anti-gp120 HIV vaccine also failed in efficacy studies (note that gp120 has long been considered to be one of the best targets for an HIV vaccine). Clearly then, the vaccines of the instant claims, which would encompass a vaccine comprising any "inactivated viral particle", which would encompass an HIV vaccine, must be considered to be highly unpredictable and requiring of undue experimentation.

Other pathogens have proven just as difficult to vaccinate against, see for example Hagan et al. (2003) wherein it is taught that *Schistosoma* parasites resist even the most effective vaccines designed using the best characterized antigens. Indeed, once again the concept of antigen vaccination has been called into question and may not prove technically feasible given the finding that repeated exposure to the organism fails to induce protective immunity (as happens with most viral and bacterial antigens, see particularly page 1273, column 1, second paragraph).

It is the Examiner's position then that this limited disclosure is insufficient support for the vaccines of the instant claims. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples, the unpredictability of physiological activity, the lack of sufficient specific guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's arguments, filed 2/17/04, have been fully considered but they are not persuasive. Note again that the rejection as it regards how to make the vaccines of the instant claims has been withdrawn, accordingly, remarks and arguments traversing said how-to-make rejection have been rendered moot and will not be addressed.

Applicant argues, "As is clear from the appealed claims of Groups I, II, and III, the present invention is characterized by the addition of a polyethylene glycol derivative to the outer aqueous phase of a W/O/W type oil adjuvant vaccine...The novel feature of the present invention involves the presence of the polyethylene glycol derivative in the outer aqueous phase of a W/O/W type emulsion and not on the *specific antigen used.*"

It is clear then that Applicant intends the vaccines of the instant claims to encompass the use of any and all possible antigens. For the reasons set forth above, said vaccines are not enabled by the instant specification.

Applicant asserts, "As is clear from the description of the present invention recited in the specification of the present application, the identity of the antigen - within reason - is not

important to the preparation and use of the present invention, which involves the addition of a polyethylene glycol derivative to the outer aqueous phase of otherwise well-known W/O/W type oil adjuvant vaccines. The Examiner has not set forth *any* evidence or reasonable arguments to the contrary, i.e., that demonstrate that identity of the antigen is critical to the preparation and use of the present invention and that such antigens are not disclosed in the present application in a manner to enable the preparation of the present invention as defined by the appealed claims of Group I, II, or III"

Applicant's assertions regarding the use of the claimed vaccines is not supported by the facts and evidence now set forth above by the Examiner.

Applicant argues, "Moreover, Appellants need not exemplify each and every embodiment of the claimed invention. Appellants need only teach those of ordinary skill in the art how to make and use the present invention."

Applicant is advised that a specification, enabling of the scope of the invention of the instant claims, is required. While the instant specification *may* be enabling for a W/O/W adjuvant, the invention of the instant claims is a vaccine which is not enabled by the instant specification.

5. Claims 1-17 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, for the reasons of record. As set forth in the paper mailed 11/01/02:

"There is insufficient written description to show that Applicant was in possession of a W/O/W type oil adjuvant vaccine as recited in the claims. The specification discloses an essentially indecipherable method for producing the vaccines encompassed by the instant claims (see paragraph 3). Said method additionally fails to disclose the specific components of any of the vaccines encompassed by the instant claims. The mere recitation of vague limitations such as a PEG phase of between 0.5 - 20% wt% (Claim 1), or an oil phase component which becomes liquid at room temperature (Claim 4), or an emulsifier which has an HLB of less than 10 (Claim 12), is insufficient to describe the vaccines of the instant claims. Additionally, given the breadth of the claims (see paragraph 3), one of skill in the art

must conclude then that the specification fails to disclose a representative number of species to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398."

Applicant's arguments, filed 2/17/04, have been fully considered but they are not persuasive. Applicant does not argue the rejection independently, but argues that the specification provides a sufficient written description such that one of ordinary skill in the art could make and use the vaccines embodied by the pending claims.

It is the Examiner's position the single vaccine disclosed in the specification cannot be considered to be a representative number of species of the claimed genus of vaccines. As set forth above, the instant claims are drawn to vaccines and not an adjuvant. Consider the example of HIV vaccines; no antigens capable of inducing an effective immune response are currently known, yet Applicant makes clear in the arguments that there exist no limitations on the vaccines of the instant claims. Accordingly, the rejection has been maintained.

6. Claims 1-17 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection. As set forth previously:

"The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:
A) The phrase, "wherein the inner aqueous phase is <u>discontinuous and suspended</u> in the oil component phase, and the oil component phase is <u>discontinuous and suspended</u> in the outer aqueous phase" in Claim 1, comprises a limitation not supported by the specification or claims as filed."

Applicant's arguments, filed 2/17/04, have been fully considered but they are not persuasive. Applicant indicates that "While the literal terms "discontinuous and suspended" are not present in the specification of the present application, one of ordinary skill in the art would recognize that the specification description of the inner aqueous phase as a dispersion phase in the oil component phase of the emulsion necessarily means that the inner aqueous phase is "discontinuous and suspended" in the oil component phase".

Applicant is advised that if the term means only that which is disclosed in the specification, Applicant could obviate the rejection by using the language of the specification, or in the alternative, not reciting in the claims that which is unnecessary as it is inherent to the claimed vaccines.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

9. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

4/26/04

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